

Comparison between Computed Tomography & Fluoroscopy Guided Facet Joint Block in Lumbar Spine

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Abstract

Background Data: Facet joint disorders are main source of chronic low back pain with a prevalence of 16.7%. Facet joint block is performed for diagnostic or therapeutic purposes and generally is carried out under computed tomography (CT) or fluoroscopy. Facet joint block is the gold standard in diagnosis of facet joint syndrome. It can also relief pain for up to 6 months.

Purpose: To identify which imaging modality (CT or fluoroscopy) is more suitable to guide the procedure of lumbar facet joint block, and results in better relieve of symptoms.

Study Design: Prospective analytic clinical case study.

Patients and Methods: Sixty eight lumbar facet joints representing 24 patients were injected in the radiology department, Suez Canal University Hospital, Ismailia, Egypt from 1/2005 to 12/2010. All cases were suspected of having facet joint disorders based on clinical and radiological data. After clinical examination and reviewing lumbar images to identify target facets, every patient underwent facet joint block under either CT or fluoroscopy. Visual Analogue Scale was used to assess improvement of symptoms.

Results: Fluoroscopy was more successful in guiding the injections (success rate 77.7% compared with 31.25% in CT guidance). It is also faster (6:37 minutes per joint compared with 10:54 minutes for CT guidance). Less number of trials were required (1.7 trial compared with 6.6 trials with CT guidance). Fluoroscopy exposed the patients and the radiologist to much irradiation (21.3 rad compared to 0.3 rad in CT guidance). Decreased bone density and laminectomy impair fluoroscopy guidance. CT guidance is difficult in patient with marked arthropathy and coronally oriented joints (8 trials compared with 5.6 for normally appearing joints). Both groups showed significant improvement of symptoms.

Conclusion: Fluoroscopy should be the primary choice for guiding lumbar facet joint block. It is more successful and faster. Its disadvantages include much irradiation to patients and radiologists, and difficulty in patients with laminectomy and decreased bone density. CT can then be used to guide the block. Both techniques are effective in pain reduction. (2012ESJ035)

Key Words: Lumbar facet joint block, facet syndrome, Fluoroscopy, Computed tomography.

Introduction

Facet joint arthropathy is a main cause of chronic low back pain. The prevalence of lumbar facet joint mediated pain is 16.7%.¹⁵ Role of examination and imaging in identifying facet joints as a main source of pain is limited and unreliable and may diagnose only 30% of cases with a false positive diagnosis up to 45%. CT has limited place in proving that a particular facet joint is the main source of patient pain: Degenerative changes seen by CT may not be painful, and facet pathology may be present despite normal CT morphology.^{21,22}

Several pathological processes can affect the facet joint: congenital hypoplasia or maldirection, degeneration, facet joint defects, synovial cyst, abnormal communications with the contralateral facet through a pathological interspinous bursa, or subjacent facets through pars defect, trauma, micro-trauma, iatrogenic reduction, meniscoid entrapment, synovial impingement, joint subluxation, chondromalacia facette, systemic inflammatory arthropathies, mechanical injury to the joint's capsule, and restriction to normal articular motion from soft or articular causes.^{16,7}

Clinical criteria for diagnosis of patients with facet joint mediated pain may not be reliable to diagnose and identify the exact pathological level. It provides a 45% false positive. Criteria include pain not exacerbated by coughing, pain increased by recumbence, relieved by walking, deep achy nature, no parasthesia or no root tension signs, pain provocation by pushing hips forward while standing, morning stiffness with stooped posture, no radiation below knee, well localized paraspinal tenderness, pain in the back with straight leg raising test, pain with extension and rotation toward the symptomatic side.¹⁹

Facet joint block has a major diagnostic value. No matter what the symptoms, signs or imaging features are, a characteristic feature of facet syndrome is relief of pain from injection of local anaesthetic.² Indeed, facet joint arthrography, performed as a part of facet joint block under fluoroscopy, shows a higher sensitivity for joint degeneration than CT.²⁰

The primary treatments for lower back pain commonly include bed rest, medication and physiotherapy. Despite these treatments, there are many cases in which the chronic disease progresses

without improvement of symptoms.⁵ Therapeutic value of facet joint block to patients with chronic low back pain has been proved. More than 18% of cases of chronic low back pain show complete relief of pain for 6-12 months, and 12 % of them show complete disappearance of lower extremity pain but not low back pain.¹

There are several techniques to block the lumbar facet joints. Blind techniques are done in pain clinics.¹⁸ Intra-articular injection can be performed under fluoroscopy or CT guidance.^{8,9} Medial branch block can be performed using radiofrequency or pharmacologically.^{3,6,10,12}

Complications of facet joint injection include: 2.6% transient increase in pain, 0.9% transient radiculopathy, 1.3% puncturing the dura with transient headache. Intravascular injections, side effects of steroids, contrast or anesthetics are rare complications. Septic arthritis is also rare after facet injection.^{1,13,14,17}

This study was designed to identify which imaging modality is more suitable to guide the procedure of lumbar facet joint block, fluoroscopy or computed tomography. Symptoms improvement is also compared between the two approaches. The following parameters were chosen: radiation exposure, number of trials, execution time, success rate, and extra-articular spill. For outcome assessment, Visual Analogue Scale (VAS) was used.

Patients and Methods

The study was performed in Neurosurgery and Radiology Departments, at Suez Canal University Hospital, Ismailia, Egypt from January 2005 to December 2010. Sixty eight lumbar facet joints represented by twenty four patients were injected.

Inclusion criteria include: 1) clinical suspicion of facet joint syndrome, 2) radiological suspicion of facet joint pathology such as single level, single facet, facet defect, synovial cyst, iatrogenic reduction of facet joint, 3) prior to disc surgery if facet component of pain is suspected, acute post-operative low back pain or pseudo-radicular pain and failed back surgery syndrome⁴, and 4) as a part of interventional workup for patient with chronic low back pain with no identifiable cause.

Exclusion criteria include: 1) allergy to steroids, contrast or anesthetics, 2) coagulopathy, 3) severe lumbar canal stenosis as it may provoke edema and

more stenosis, 4) pregnancy, and 5) skin sepsis over the target region.

Facet joint block was done under computed tomography using CT Seimens Somatom Balance (Germany) or fluoroscopy using Angiography unit Philips Integris X-Ray Machine (Holland).

Every patient underwent medical history, clinical examination in addition to reviewing lumbar images. The following data was collected: age, sex, indications, level, previous spinal operations, facet osteoarthritis, execution time, number of trials, success, and contrast spill. Calculating the dose of irradiation was done automatically by the CT device. Regarding fluoroscopy, average patient exposure guides were used.²⁶

Visual Analogue Scale (VAS) was used to assess improvement of symptoms. VAS score was measured before and after the procedure. The patients had 30-minutes of bed rest and any abnormalities were confirmed. Assessment of VAS was done at 1, 3, and 6 months follow-up visits.

The injected medications included: 1) Non-neurotoxic contrast: iohexol 300 mg/ml iodine (Omnipaque), 2) Sustained action steroid: Triamcinolone acetonide (Kenacort A) and Methylprednisolone (DepoMedrol). 3) Long acting Anesthetic: 0.5% Bupivacaine hydrochloride (Marcaine).

Selecting target facet joint was done depending on clinical and radiological data (most tender point, abnormal joints, unilaterally affected joints, single level joint affection, facet joint defects and dysplastic joints).⁸

Fluoroscopy-Guided Technique:

Figure (1) shows the inferior articular recess in the oblique view. However, the posterior approach was used by entering this recess. The patient is placed prone with no need for rotating the patient as in the oblique approach. Osteophytes do not impair the process. Indeed, degenerative changes result is an even bigger and easier recess.²⁰

Identifying the inferior synovial recess is done using bony landmark that is the tip of the inferior articular process (Figure 2). The upper medial aspect of the pedicle can be used in cases of improper visualization of the articular process due to osteopenia or obesity.²⁰

The patient is placed prone, with pillow under the abdomen to reduce the lumbar lordosis.

Under aseptic conditions a 22 gauge; a 10 cm spinal needle is directed parallel to the X-ray beam towards the tip of the inferior articular process. Usually the sensation of entering the joint capsule can be perceived. Confirming the location is done by injecting 0.5 ml contrast. Frontal and oblique arthrographs are obtained for documentation and diagnostic purposes. Half to 1 ml of anesthetic is injection followed by the same dose of steroids. For the effects and side effects, watching the patient for 15 minutes is usually sufficient. Figure (3) shows normal arthrograms of lumbar facet joint.

CT guided intra-articular injection:

Instead of targeting the inferior articular recess, the space between the two articular processes is targeted (Figure 4). Either direct posterior or oblique approach is used according to the orientation of the facet joint. Otherwise the procedure is similar to fluoroscopy guided technique²⁴

Results

Sixty eight lumbar facet joints represented by twenty four patients were injected. Thirty two facets were injected using CT-guidance, while 36 facets were injected under fluoroscopy. Age ranged between 25 and 75 years with a mean of 45 years. Male patient represented 65% of the sample, contributing to 68% of the facets joints. A mean number of 2.8% facet joints were injected for every patient.

Indications for injection:

Facet joint syndrome was indicated for injection in 25 facets (36.8%), diffuse disc bulge with atypical pain in 17 facets (25%), disc herniation with atypical sciatica in 13 facets (19.1%), failed back surgery syndrome in 11 facets (16.2%), and unilateral facet joint arthropathy in 2 facets (2.9%). The most prolonged fluoroscopy guided injections were in patients with failed back surgery syndrome with an average execution time of 8:45 minutes per facet joint, compared to 4:30 minutes only for patients with facet joint syndrome (Table 1). P-value <0.05. Failed back surgery syndrome showed the largest dose of irradiation to the patients with a mean entrance skin exposure of 25.82 rad per facet joint compared to 0.26625 rad for those facets injected due to diffuse disc bulge with atypical sciatica, and 18.22 rad for facet syndrome. P-value <0.01.

Level of the injected facet joints and number of trials:

L4-L5 level was the most frequently chosen levels for injection representing 63.2 % of the injected facet joints. L2-L3 and L3-L4 were the least chosen level (5.9% each). L2-L3 level showed the least average number of trials (one trial), while L3-4 showed the highest number (eight trials), using fluoroscopy. P-value > 0.05. (Table 2, Graph 1)

The impact of gross arthropathic changes on the CT guided blocks:

Forty four % of the facets injected under CT had CT features of arthropathy (14 facets). The mean number of trials under computed tomography was 8 trials among those patients compared with 5.6 trials for those patients with normally appearing facets by CT. P-value < 0.05. (Table 3)

Success of gaining an intra-articular access:

Gaining an intra-articular access was successful in 77.7 % of those facets injected under fluoroscopy and in 31.25 % of those injected under computed tomography. P-value < 0.01. Excessive extra-articular leak was the cause of failure of fluoroscopy guidance in 6 over 36 facets. (Table 4)

Execution time and number of trials:

The mean execution time per facet joint was 6:37 minutes for fluoroscopy guidance compared to 10:54 minutes for CT guidance. P-value =0.01. Number of performed trials to gain access to the facet joint was higher using CT guidance with a mean of 6.9 trials compared to a mean of 1.75 trials for fluoroscopy guidance (Graph 2). P-value < 0.01. The most prolonged CT guided procedures were for those patients with facet joint arthropathy with a mean of 22 min compared to 9.3 minutes for patients with diffuse disc bulge and atypical pain. P-value < 0.05.

Radiation exposure to the patients:



Figure (1). Diagram of lumbar facet joint (oblique view) illustrates the inferior articular recess (arrow) (Quoted from Sarazin et al, 1999)²⁰

Entrance skin radiation exposure for patients was much higher when fluoroscopy is used with a mean of 21.3 rad compared to 0.30 rad using computed tomography. P-value < 0.01. (Graph 3)

Bone density and fluoroscopy guidance:

Decreased bone density was subjectively noted in 22.58% of facet joints. This was the reason for difficult procedures in 11.7 % of fluoroscopically injected facets joints. Indeed, 50 % of fluoroscopy guided injections in patients with osteoporosis was not successful and all facets with normally appearing density was successful.

Assessment of improvement after injection:

Visual analogue scale was used to assess improvement of pain after injection. It was measured before injection, first day before discharge, and at 1, 3, and 6 months interval. In CT-guided group, VAS score significantly improved from 7.7 points before injection to 3.3 points at final follow up visit (P<0.05). In the fluoroscopy-guided group, VAS score significantly improved from 7.9 points before injection to 3.4 points at final follow up visit (P<0.05). There was no significant difference between both groups (Table 5).

Complications after facet joint block:

There were some cases with self-limited symptoms as aggravation of low back or limb pain, tingling sensation, and allergic reaction. These symptoms occurred in 5 cases of CT-guided group and 4 cases in fluoroscopy-guided group (total 13.2% of cases). There were two cases with superficial infection (2.9%) that improved within 2 weeks. Two patients (2.9%) developed mild lower limb weakness that improved at 1-month follow-up visit. There was no statistically significant difference in the incidence of complications between the two groups.

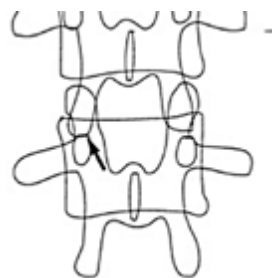


Figure (2). The location of the puncture site is under the tip of the inferior facet (arrow). Note that the site is located at the medial projection of the pedicle. (Quoted from Sarazin et al, 1999)²⁰

Figure (3). Posteroanterior and lateral lumbar facet joint arthrograms demonstrate normal anatomy. Note the smooth ring appearance of the joint (arrowheads) and the S-shaped appearance (arrow).

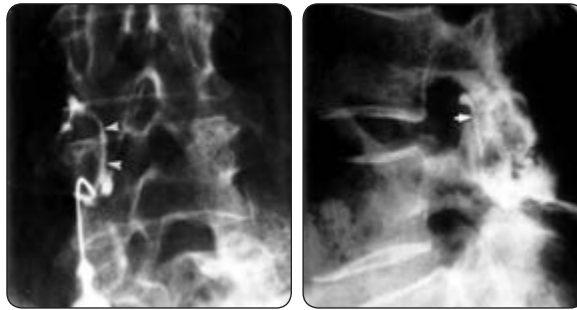


Figure (4). Axial CT with spinal needle inside the facet joint space, patient is prone. Contrast is seen inside the joint space and synovial recesses.

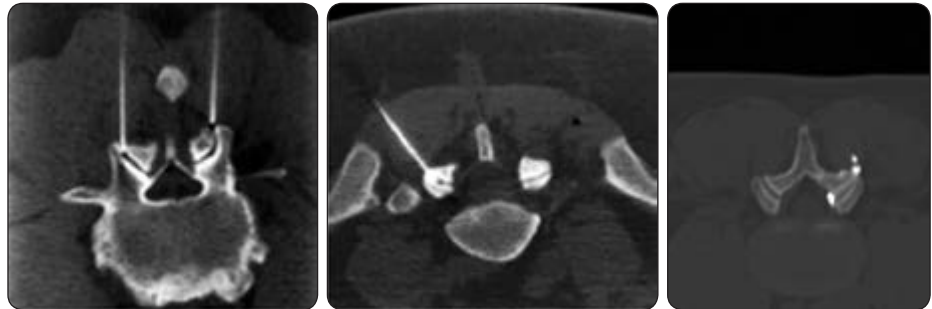


Table (1). Execution Time Correlated with Indication of Injection.

Average execution time	
Facet syndrome	4:30 min
Failed surgery syndrome	8:45 min

Table (2). Number of Trials Correlated With Different Levels of Injection.

	Number of joints	%	Average number of trials
L2-L3	4	5.9	1
L3-L4	4	5.9	8
L4-L5	43	63.2	3.9
L5-S1	17	25	4.9

P>0.05

Table (3). Number of computed tomographic guided trials: arthropathic joints versus normally appearing joints by CT.

	Number of joints	Average number of trials
Arthropathic joints	14	8
Normally appearing joints	18	5.66
	32	

P<0.05

Table (4). Success Rate in Computed Tomography Guided and Fluoroscopy Guided Techniques.

	Number of injected joints	Number of successful injection	Success rate %
Success rate %	32	10	31.25
Fluoroscopy	36	28	77.77
Total	68	38	

P<0.01

Table (5). Visual Analogue Scale (VAS) Score after Facet Block.

	Before procedure	After Injectioa	1 month	2 months	3 months
CT-guided group	7.7	3.2	2.2	2.9	3.3
Fluoroscopy group	7.9	3.5	2.3	2.2	3.4

Discussion

Fluoroscopy is still the most common method of guiding facet joint block. Since the advent of CT, and more recently CT fluoroscopy, these modalities are beginning to be more widely used to direct facet joint blocks.²⁵ Proponents of fluoroscopy cite decreased procedure time and cost, whereas CT offers the advantages of no contrast material, more precise needle tip placement, and visualization of important vascular structures. Time limitations often prevent the use of traditional CT guidance, especially in busier units, but with CT fluoroscopy, the time differences between the two techniques are diminished markedly. The cost differential between the two techniques is 0.6 relative value units, and this should be taken into account when a technique is chosen.²⁵

Sixty eight facet joints were included in the study represented by twenty four patients. A mean of 2.8 facets were injected in every patient, approximately similar to what was done in Bani et al. 5 years works (3.1 facet joint per patient) through injecting 715 facets of 230 patients.¹ The age ranged between 25-75 years old with mean age of 45 years. The most common age incidence of facet joint syndrome is around 59 years. Bani et al,²³ work showed an age range between 32 and 81 years with a mean age of 55 years.¹

Our study purpose is to compare fluoroscopy and CT as image guidance to facet joint block. The following parameters were used for comparison: radiation exposure, number of trials, execution time, success rate and extra-articular spill. Improvement of symptoms was also compared using VAS. Studies found in literatures concentrated on the value of facet joint block in diagnosing and eliminating facet mediated pain¹ as well as setting clinical criteria for subjecting patient with low back pain to such an invasive test.¹⁹ No previous studies could be found comparing between these two modalities.

Male patients represented 65% of the sample, in agreement with previous studies which showed increased incidence of this syndrome in males.¹ L4-L5 level was the most frequently chosen level for injection representing 63.2% of the injected facet joints followed by L5-S1 level (25%). L2-L3 and L3-L4 levels were the least injected levels, each representing 5.9% of the sample. The lower the

injected level is, the more difficult to access the joint space under CT due to the more coronal orientation of the facets caudally. This distribution of target facets seems to follow the incidence of facet joint mediated pain; the following is the spinal levels treated with block in Bani et al,¹ work in 2002: L5-S1 level unilaterally (25.7%), L4-L5 unilaterally (21.3%), L5-S1 level bilaterally (19.1%), L4-L5 level bilaterally (6%) and L3-L4 level unilaterally (5.2%).

It was noticed that fluoroscopy guided procedures was prolonged when done to patients with laminectomy (16.2 % of the sample) with an average execution time of 8.75 minutes per facet joint compared to 4 minutes only for patients with facet joint syndrome. This could be explained by decreased articular facet density, anatomical distortion, reduced facets, and painful scar associated with laminectomy. Also, the deliberate avoidance to puncture the exposed dura may make the procedure more prolonged. Indeed, those patients with laminectomy are exposed to more irradiation than others, with a mean entrance skin exposure of 25.82 rad per facet joint compared to 0.2668 rad for diffuse disc bulge with atypical manifestations.

Injecting the grossly arthropathic joint under CT was more difficult, with mean number of trials reaching 8 trials compared to 5.6 trials only for normally appearing facet joint. This was in agreement to Sarazin et al,²⁰ who stated in 1999 that direct access to the lumbar facet joint space is not always possible owing to degenerative changes such as osteophytes.

Fluoroscopy guidance exposes the patients to higher doses of irradiation (mean value 21.3 rad entrance skin exposure) than CT guidance (mean value 0.3 rad entrance skin exposure). Fluoroscopic screen takes the upper hand for such high dose sharing in 92.7 % of the mean entrance skin exposure dose to those patients. Needless to say, radiologist's irradiation dose is nil during injection under computed tomography, this adds a great advantage to it. Fluoroscopy was more successful than CT for guidance: the success rate was 77.7% and 31.25% respectively. It was stated that the procedure of inserting the needle into the inferior articular recess is much easier than inserting the needle into the joint space.²⁰

Facet joint injection under fluoroscopy was faster than injection under computed tomography, with

mean execution time of 6:37 minutes and 10:54 minutes per facet joint respectively. Also the mean number of trials was 1.75 and 6.9 trials per facet respectively. Fluoroscopy offers to the radiologist a real time image which allows easy and fast redirection of the needle. Also, the inferior synovial recess is a larger and easier target to each than the narrow, sometimes obliterated or markedly coronally oriented lip of the facet joint. This explains the previous results.

Considerable extra-articular leak was the cause of failure of fluoroscopy (6 out of 36 facets). Sarazin et al,²⁰ reported a success rate of 90 % in fluoroscopy guided technique, 6% capsular leak and 4% failure to insert the needle at the inferior articular recess. They reported that these statistical data were collected over 10 years obtaining more than 15000 lumbar facet arthrograms. They must have had major experience in such technique in contrast to the rising learning curve for the operator of this study. This could explain the difference in results.

There was a significant improvement of pain in both groups when comparing the VAS before and after the procedure and at the 1st, 3rd, and 6th month's follow-up visit. Furthermore, there was no significant difference between both groups. This is similar to the results of Ha DH et al. Their study compared also the ultrasonography-guided facet block to fluoroscopy.¹¹

There were no major complications of facet joint block in this study. Complications included aggravation of low back pain, tingling, allergic reaction, superficial infection and mild lower limb weakness of limited duration. Other studies confirmed also that minor side effects are common after facet joint injection and major complication are extremely rare.¹⁴

Conclusion

We conclude that fluoroscopy should be the primary choice for guiding lumbar facet joint block. It is more successful, faster, with less number of trials required compared to CT guidance. Its disadvantages include; much irradiation to the patient and the radiologist than CT, and difficulty in patients with decreased bone density and laminectomy.

The following could explain the feasibility of fluoroscopy guidance: real time, synovial recess is a larger target, arthropathy enlarge the inferior recess, osteophytes does not impair the process,

joint narrowing does not impair the process, coronal orientation of the joint space does not impair the process. CT guidance is more difficult especially for arthropathic joints and coronally oriented joints. It should be reserved for patients with laminectomy, decreased bone density, cases of failed fluoroscopy guided injection and for radiologists who wish to keep the dose of irradiation to a minimum. Both techniques are significantly effective in reducing low back pain with minor complications.

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الملخص العربي

مقارنة بين الاسترشاد بالأشعة المقطعية بالحاسب الآلي أو الاسترشاد بالملصاف في تخدير المفصل السطحي القطني

مقدمة: تمثل أمراض المفصل السطحي مصدراً أساسياً للآلام أسفل الظهر المزمنة بنسبة تصل إلى ١٦.٧٪. ويتم تخدير المفصل السطحي القطني للتشخيص وللعلاج وذلك باستخدام الأشعة المقطعية بالحاسب الآلي أو باستخدام الملصاف للتصوير الاسترشادي. ويعتبر تخدير المفصل السطحي الطريقة المعيارية الذهبية لتشخيص متلازمة المفصل السطحي. بالإضافة إلى ذلك فإنه يؤدي إلى تخفيف الآلام لفترة تصل إلى ستة أشهر.

الهدف: المقارنة بين الملصاف والأشعة المقطعية بالكومبيوتر كوسيلة إرشادية لحقن المفصل السطحي القطني والحصول على تخفيف أفضل للأعراض.

الطرق: أدرج ٦٨ مفصل سطحي قطني في هذه الدراسة ممثلين في ٢٤ مريضاً من قسم جراحة المخ والأعصاب وتمت الدراسة بقسم الأشعة بمستشفى جامعة قناة السويس بالإسماعيلية بمصر في الفترة من يناير ٢٠٠٥ وحتى ديسمبر ٢٠١٠. كل المرضى تم اختيارهم بناء على المعلومات الإكلينيكية والإشعاعية التي تؤكد وجود أمراض المفاصل السطحية لديهم. وبعد إجراء الفحص الإكلينيكي والاطلاع على الصور لتحديد المفاصل المطلوب حقنها، تم إجراء الحقن باستخدام الأشعة المقطعية بالحاسب الآلي أو باستخدام الملصاف للتصوير الاسترشادي. وتم تقييم مدى التحسن باستخدام المقياس التمثيلي البصري.

النتائج: كان الملصاف هو الأنجح في الإرشاد إلى دخول تجويف المفصل وبلغت نسبة النجاح ٧٧.٧٪ مقابل ٣١.٢٥٪ لاستخدام جهاز الأشعة المقطعية. ويعتبر الملصاف الأسرع أيضاً حيث بلغ متوسط الزمن المستغرق لدخول المفصل ٦:٣٧ دقيقة تحت الملصاف مقابل ١٠:٥٤ دقيقة باستخدام المقطعية. وكانت عدد مرات المحاولات لدخول تجويف المفصل في المتوسط ١.٧ محاولة في حالة الملصاف مقارنة بعدد ٦.٦ محاولة في حالة الأشعة المقطعية. وتكمن عيوب الملصاف في جرعات الإشعاع العالية التي يتعرض لها الطبيب والمريض والتي بلغت في المتوسط ٢١.٣ راد مقابل ٠.٣ راد للمقطعية. كما لوحظ أن انخفاض كثافة عظام المفاصل أو المفاصل التي أجريت بجوارها عمليات جراحية تعوق من الاسترشاد بالملصاف في الحقن. ومن الناحية الأخرى فإن الاسترشاد بجهاز الأشعة المقطعية في الحقن يكون على قدر من الصعوبة في حالات وجود خشونة أو تغيرات باثولوجية أخرى حيث تعوق النتوءات العظمية مسار إبرة التخدير. تمثل ذلك في عدد المحاولات لتصل في المتوسط إلى ٨ محاولات للمفصل المتآكل في مقابل ٥.٦ محاولة للمفصل ذو المظهر الطبيعي. لوحظ كذلك أن كلتا المجموعتين أظهرتا تحسن ذو دلالة إحصائية في الأعراض.

الاستنتاج: نستخلص من هذه الدراسة أن الملصاف يجب أن يكون الاختيار الأول للإرشاد لتخدير المفاصل السطحية القطنية. حيث أنه الأسرع والأنجح. ويعيبه كثرة التعرض للإشعاع وعدم قدرته على الإرشاد للمفاصل ذات العظم الهش أو التي أجريت بجوارها عمليات جراحية. عندئذ يمكن استخدام جهاز الأشعة المقطعية للإرشاد للحقن. كما أن كلتا الطريقتين تؤديان إلى تحسن ملحوظ في الأعراض.